

CLAIMS

We claim:

1. A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to a NOR1 gene;
 - (b) a second polynucleotide sequence homologous to the NOR1 gene; and
 - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a NOR1 gene;
 - (b) providing a second polynucleotide sequence homologous to the NOR1;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of the NOR1 gene and a second sequence homologous to the NOR1 gene; and
 - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
5. A cell comprising a disruption in a NOR1 gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a NOR1 gene.
9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in the NOR1 gene, the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression or function of NOR1, the method comprising:

- (a) providing a non-human transgenic animal comprising a disruption in a NOR1 gene;
- (b) administering an agent to the non-human transgenic animal; and
- (c) determining whether the expression or function of NOR1 in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the expression or function of NOR1, the method comprising:

- (a) providing a cell comprising a disruption in a NOR1 gene;
- (b) contacting the cell with an agent; and
- (c) determining whether expression or function of NOR1 is modulated.

13. An agent identified by the method of claim 11 and claim 12.

~~14.~~ The non-human transgenic animal of claim 8, wherein the transgenic animal exhibits increased or enhanced pain response threshold.

~~15.~~ The non-human transgenic animal of claim 8, wherein the transgenic animal exhibits impaired balance and impaired motor coordination.

16. A method of identifying an agent that ameliorates impaired balance and motor coordination, the method comprising administering an agent to the non-human transgenic animal of claim 15 and determining whether the agent ameliorates impaired balance and motor coordination.

17. A method of identifying an agent that improves balance and motor coordination, the method comprising administering an agent to the non-human transgenic animal of claim 15 and determining whether the agent ameliorates impaired balance and motor coordination.

~~18.~~ A transgenic mouse comprising a disruption in a NOR1 gene, wherein the transgenic mouse exhibits increased or enhanced pain response threshold.

~~19.~~ A transgenic mouse comprising a disruption in a NOR1 gene, wherein the transgenic mouse exhibits impaired balance and impaired motor coordination.

20. A method of identifying an agent that affects a phenotype associated with a disruption in a NOR1 gene, the method comprising:

- (a) providing a transgenic mouse comprising a disruption in a NOR1 gene;

- (b) administering an agent to the transgenic mouse; and
- (c) determining whether agent affects a phenotype in the non-human transgenic animal, wherein the phenotype is increased or enhanced pain response threshold or impaired balance and impaired motor coordination.
21. A method of identifying an agent that modulates the expression or function of NOR1, the method comprising:
- (a) providing a transgenic mouse comprising a disruption in a NOR1 gene;
 - (b) administering an agent to the transgenic mouse; and
 - (c) determining whether agent modulates the expression or function; wherein the agent modulates enhanced pain response threshold or impaired balance and impaired motor coordination.
22. A method of identifying a compound that inhibits the activity of NOR1, the method comprising:
- (a) providing a cell expressing NOR1;
 - (b) contacting the cell with a test compound; and
 - (c) determining whether the activity of NOR1 is decreased in the presence of the compound.
23. An agent identified by the method of claim 16, claim 17, claim 20, claim 21, or claim 22.
24. A method of ameliorating impaired balance or impaired motor coordination, the method comprising administering to a subject in need a therapeutically effective amount of NOR1.
25. A method of improving balance and motor coordination, the method comprising administering to a subject in need a therapeutically effective amount of NOR1.
26. A pharmaceutical composition comprising NOR1.